Abstract

Background

Advances in the oncological and functional results of insular surgery have been reported recently. Such successes have been made possible by the advent of the transopercular approach under awake monitoring and by the improved anatomical and functional knowledge of the white matter pathways surrounding the insula. Nonetheless, given the rarity of insular tumors, it is difficult to get familiar with the complex 3D anatomy of the different neuronal and vascular structures encountered during a transopercular insular resection. We thus propose to develop a laboratory model allowing to train transopercular approaches of the insula

Methods

Two hemispheres prepared with Klinger's technique were dissected under light microscope, preserving all pial membranes. The different steps of the dissection were video recorded.

Results

The preservation of pial membranes enabled to simulate subpial resection, both during operculum removal and during insular cortex resection. The medial wall of the resection was defined by the inferior-fronto-occipital fasiculus, protecting from the lenticulostriate arteries.

Conclusion

In this paper, we show that Klinger dissection with preservation of pial membranes provides a realistic model of insular surgery, allowing to learn and train this highly-specialized surgery.

Key words : anatomy, insula, surgery, neuronavigation, subpial dissection, fiber dissection

Introduction

Removal of insular tumors requires a highly-specialized neurosurgical expertise [1]. The insula is burried within highly eloquent operculum and is surrounded by equally essential vascular structures [2,3]. Moreover, the deeper boudaries of the resection include medially the uncinate fasciculus (UF), the inferior fronto-occipital fasciculus (IFOF) and the putamen, which are highy functional structures, and, ventrally and inferiorly, the anterior perforate substance (APS), the most risky zone regarding perforating arteries. The classical route towards the insula was through the opening of the sylvian fissure [4,5]. This is geometrically the shortest path from the surface towards the insula. It nevertheless carries a risk of injury or vasospasm of M2/M3 branches arising from the middle cerebral artery [6–8]. Consequently, the transopercular approach under cognitive monitoring in an awake patient has gained more and more interest [8–12]. First, it allows to remain subpially to the vessels running on the insular surface, thus minimizing the risk of injury to M2/M3 arteries and veins. Second, the exposure has been shown to be much wider after operculum removal, rather than through the transylvian approach [13], thus reducing opercular retraction.

On the top of all these difficulties, the rarity of insular tumors limits the opportunities to get familiar with the complex 3D vascular and functional anatomy of this region. As a consequence, simulating insular surgery at the laboratory might be the only way to train and acquire the knowledge that is required before going to the operative theater for an insular tumor case. In this paper, we demonstrate the feasability of the transopercular approach in Klinger prepared brain specimen, with special emphasis on subpial dissection and IFOF identification.

Methods

Freshly specimen were immersed in 10% formalin solution for at least 3 weeks. These specimen were freezed at -18°c for 2 weeks. Defreezing was done at room temperature. A 3T MRI with 3D-

T1 (TR=2000 ms, TE = 2.68 ms, voxel size = 1x1x1 mm) and 3D-T2 (TR=2800 ms , TE = 416 ms, voxel size = 1x1x1 mm) sequences was performed, after magnetic fiducials were tacked up (see first sequence of video 1a & 1b). The tracker was stiched to the tentorium, just above the cerebellar surface. Point-based registration was achieved using the Axiem of the Treon station (Medtronic), thus allowing to navigate during the dissection. The dissection was performed under the light of the microscope (OPMI pico Karl Zeiss, inc. Oberkochen, Germany), and video recorded with a HD-camera (Karl Storz GmbH, Tuttlingen, Germany). Video editing was achieved with iMovie (Apple). Two versions were produced: in the first ones (video 1a & 2a), we kept the genuine angle of view, that was found the most convenient for performing the dissection, while in the second ones (video 1b & 2b), sequences were rotated in such a way that the angle of view was made similar to the surgical one (that is with the head in a neutral lateral positioning).

Results

Two hemispheres (one right – video1 and one left – video2) were dissected. First, to help visualize where the insular boundaries would project onto the lateral surface of the brain, we used the neuronavigated pointer, with varying in-depth view. We thus were able to delineate the projection onto the surface of the anterior, superior and inferior limiting sulcus, allowing to study the relationship between these projections and the precentral, central and postcentral sulcus, the sylvian fissure, and the superior temporal sulcus. These projections are usefull to built a mental picture of where the insula is located. Before starting dissection, precentral gyrus and inferior frontal sulcus are identified, allowing to delineate the posterior part of the inferior frontal gyrus. The next landmarks are the ascending and horizontal branches of the sylvian fissure, providing further subdivision of this region into pars opercularis, pars triangularis, and pars orbitalis.

The first step is to remove the pars triangularis. By doing so, one encounters a white matter sheet, that contains U-fibers (connecting with pars opercularis, orbitalis, middle frontal gyrus, and insula) and terminations of the IFOF [14] and, for some authors, terminations of the AF/SLF [15,16]. Following subpially the ascending branch of the sylvian fissure leads to the insular surface, with identification just anteriorly of the anterior limiting sulcus. Following a little bit further the anterior limiting sulcus in the upward direction will guide up to the anterior insular point, at the junction between the anterior and superior limiting sulcus.

In a second step, the dissection is pursued over the temporal operculum. Subpial removal of the superior temporal gyrus allows to uncover the hidden insular surface and to identify the inferior insular sulcus. Hence, at this stage, we created the frontal and temporal corridors to get access to the insula. It is worth mentionning that these two areas have fewer functionally important connections compared to the posterior frontal, parietal and temporal operculum [17].

Going back to the frontal operculum, the pial membrane of the anterior limiting sulcus is gently lifted up, allowing to start the subpial resection of the insular cortex. Anterior short gyri are resected, and going further inferiorly leads to the inferior insular sulcus, thus connecting with the cavity of the temporal operculum removal. A coronal cut is then made in the middle temporal gyrus, in order to identify the tip of the temporal horn, allowing to understand the anatomy of the temporal isthmus. After the insular cortex removal, the white matter sheet of the extreme capsule is exposed, containing inter-gyral U-fibers and insulo-opercular fibers. Just deeper, the most lateral fibers of the UF and IFOF are found antero-ventrally, embedded in the gray matter of the ventral claustrum, while claustro-cortical fiber system constitutes the most postero-dorsal part of the external capsule. Below these latter fibers, the lateral surface of the putamen is exposed.

In the second video, to better understand the anatomical relations between IFOF, temporal isthmus and ventricle, a subpial resection of the temporal pole (thus removing the anterior part of the uncinate and inferior longitudinal fasciculus) and of the temporo-mesial structures is performed. The upper limit of the amygdala resection corresponds to the optic tract. Above this level, the amygdala fuses with the globus pallidum, without any clear demarcation [18]. This upper limit also matches more anteriorly with the level of M1, hence the APS. Following from anterior to posterior the fibers of the IFOF clearly shows that these fibers belong to the temporal stem and then to the temporal isthmus, in the roof of the temporal horn. Finally, following further the sylvian artery subpially, one can remove the limen insulae, the accessory gyrus, and the transverse gyrus. Then, by removing the cortex separating the sylvian artery from the UF, one can identify the M1 perforators, arising from the initial trunk of the middle cerebral artery, just at the level of the APS.

Discussion

In this paper, we report for the first time, to our knowledge, anatomical dissections with pial membranes preservation, allowing to simulate the subpial dissections performed during opercular approaches of the insula. In particular, this technique allows to understand the complex 3D geometry of the fronto-basal, temporal, and insular pial membranes, all of which joining at the level of the trunk of the MCA. Of note, we could confirm that lateral lenticulo-striate arteries were deeper than the the sagittal plane defined by the uncinate and IFOF [19]. As there is no landmarks to identify the LSA during the subpial cortical resection along the sylvian artery from the limen insula towards the APS, it is safe to stop medially the resection in the sagittal plane defined by the IFOF (which is identified thanks to functional responses - perseverations, semantic paraphasia, anomia, asemantism - during electrostimulations in an awake patient [20–22]). Indeed, pushing the resection until identification of the lateral most LSA already carries a risk of injury to these very small vessels [4].

Brain anatomy is normally studied in books and papers (and even in neuronavigation systems) in the canonical position, with the superior convexity of a coronal view represented at the top of the image. Hence, the mental image (what has been called « brain eye ») the surgeons have about cortical and white matter anatomy is built in this canonical position. However, in the surgical position, the head is rotated 90 degrees, meaning that the surgeon has to mentally rotate the anatomical 3D image at all the steps of the surgical procedure. Training in the laboratory enables to rebuild the mental image in the surgical position. This difficulty is well illustrated by viewing the two versions of the videos (one being close to the canonical view, and the other one close to the surgical angle of view). Importantly, one can also get a 3D feeling about the antero-posterior extent of the insula and the extreme oblique light angle that is needed to remove the insular cortex underneath the unremovable parts of the operculum. Finally, we acknowledge that this model does not take into account the deformation of normal brain anatomy seen in real patient cases, either due to preoperative mass effect of the tumor buk or to intraoperative cerebrospinal fluid loss. Nonetheless, masterizing the normal fixed anatomy is a prerequisite before implementing a 3D mental representation of distorded anatomy in patient cases.

Last but not least, while neuronavigation is of little value for real brain surgery (poor anatomical accuracy given the brain shift and lack of functional information), it was found very helpful during the present dissections. With some improvements (including adequate DTI sequences in the brain specimens), the methodology that we developped here could be generalized to simulate surgical approaches to other complex white matter regions, like the criss-cross of the temporo-parietal junction [23,24]. Moreover, in a more neuroscientific perspective, it is worth noting that, this method could also become a powerful tool for correlating fiber dissections with post-mortem DTI tractography, with the aim to validate the algorithms underlying the mathematical reconstructions of the tracts.

Conclusion and perspectives

We have shown that Klinger prepared brain specimen with pial preservation provide a realistic model for simulating transopercular approach of the insula in the laboratory. Future studies could rely on better preparation of the specimen, with injection of vessels with colored ink silicone in order to get a better picture of the vessels anatomy, and better MRI imaging of the specimen with DTI sequences in order to correlate fibers and virtual dissections. This model would also be very usefull to assess whether the endoscope could be a valuable adjunct to the transopercular approach, as previously suggested [25].

Fundings : This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. Michaud K, Duffau H. Surgery of insular and paralimbic diffuse low-grade gliomas: technical considerations. *J Neurooncol*. May 2016. doi:10.1007/s11060-016-2120-2.

2. Türe U, Yaşargil DC, Al-Mefty O, Yaşargil MG. Topographic anatomy of the insular region. *J Neurosurg*. 1999;90(4):720-733. doi:10.3171/jns.1999.90.4.0720.

3. Türe U, Yaşargil MG, Al-Mefty O, Yaşargil DC. Arteries of the insula. *J Neurosurg*. 2000;92(4):676-687. doi:10.3171/jns.2000.92.4.0676.

4. Lang FF, Olansen NE, DeMonte F, et al. Surgical resection of intrinsic insular tumors: complication avoidance. *J Neurosurg*. 2001;95(4):638-650. doi:10.3171/jns.2001.95.4.0638.

5. Hentschel SJ, Lang FF. Surgical resection of intrinsic insular tumors. *Neurosurgery*. 2005;57(1 Suppl):176-183; discussion 176-183.

6. Moshel YA, Marcus JDS, Parker EC, Kelly PJ. Resection of insular gliomas: the importance of lenticulostriate artery position. *J Neurosurg*. 2008;109(5):825-834. doi:10.3171/JNS/2008/109/11/0825.

7. Saito R, Kumabe T, Kanamori M, Sonoda Y, Tominaga T. Insulo-opercular gliomas: four different natural progression patterns and implications for surgical indications. *Neurol Med Chir (Tokyo)*. 2010;50(4):286-290.

8. Duffau H. A personal consecutive series of surgically treated 51 cases of insular WHO Grade II glioma: advances and limitations. *J Neurosurg*. 2009;110(4):696-708. doi:10.3171/2008.8.JNS08741.

9. Duffau H, Capelle L, Lopes M, Faillot T, Sichez JP, Fohanno D. The insular lobe: physiopathological and surgical considerations. *Neurosurgery*. 2000;47(4):801-810; discussion 810-811.

10. Sanai N, Polley M-Y, Berger MS. Insular glioma resection: assessment of patient morbidity, survival, and tumor progression. *J Neurosurg*. 2010;112(1):1-9. doi:10.3171/2009.6.JNS0952.

11. Hervey-Jumper SL, Li J, Osorio JA, et al. Surgical assessment of the insula. Part 2: validation of the Berger-Sanai zone classification system for predicting extent of glioma resection. *J Neurosurg*. 2016;124(2):482-488. doi:10.3171/2015.4.JNS1521.

12. Martino J, Mato D, Marco de Lucas E, et al. Subcortical anatomy as an anatomical and functional landmark in insulo-opercular gliomas: implications for surgical approach to the insular region. *J Neurosurg*. 2015;123(4):1081-1092. doi:10.3171/2014.11.JNS141992.

13. Benet A, Hervey-Jumper SL, Sánchez JJG, Lawton MT, Berger MS. Surgical assessment of the insula. Part 1: surgical anatomy and morphometric analysis of the transsylvian and transcortical approaches to the insula. *J Neurosurg*. 2016;124(2):469-481. doi:10.3171/2014.12.JNS142182.

14. Sarubbo S, De Benedictis A, Maldonado IL, Basso G, Duffau H. Frontal terminations for the inferior fronto-occipital fascicle: anatomical dissection, DTI study and functional considerations on a multi-component bundle. *Brain Struct Funct*. 2013;218(1):21-37. doi:10.1007/s00429-011-0372-3.

15. Fernández-Miranda JC, Wang Y, Pathak S, Stefaneau L, Verstynen T, Yeh F-C. Asymmetry, connectivity, and segmentation of the arcuate fascicle in the human brain. *Brain Struct Funct*. March 2014. doi:10.1007/s00429-014-0751-7.

16. Wang X, Pathak S, Stefaneanu L, Yeh F-C, Li S, Fernandez-Miranda JC. Subcomponents and connectivity of the superior longitudinal fasciculus in the human brain. *Brain Struct Funct*. March 2015. doi:10.1007/s00429-015-1028-5.

17. Bucheli C, Mato D, Marco de Lucas E, García-Porrero JA, Vázquez-Barquero A, Martino J. [Insular-opercular associative tracts: Review of their anatomy and relevance for the trans-opercular approach to the insula]. *Neurocirugia (Astur)*. 2014;25(6):268-274. doi:10.1016/j.neucir.2014.07.003.

18. Wen HT, Rhoton AL, de Oliveira E, Castro LHM, Figueiredo EG, Teixeira MJ. Microsurgical anatomy of the temporal lobe: part 2--sylvian fissure region and its clinical application. *Neurosurgery*. 2009;65(6 Suppl):1-35; discussion 36. doi:10.1227/01.NEU.0000336314.20759.85.

19. Fernández-Miranda JC, Rhoton AL, Kakizawa Y, Choi C, Alvarez-Linera J. The claustrum and its projection system in the human brain: a microsurgical and tractographic anatomical study. *J Neurosurg*. 2008;108(4):764-774. doi:10.3171/JNS/2008/108/4/0764.

20. Duffau H, Gatignol P, Mandonnet E, Peruzzi P, Tzourio-Mazoyer N, Capelle L. New insights into the anatomo-functional connectivity of the semantic system: a study using cortico-subcortical electrostimulations. *Brain*. 2005;128(Pt 4):797-810. doi:10.1093/brain/awh423.

21. Duffau H, Herbet G, Moritz-Gasser S. Toward a pluri-component, multimodal, and dynamic organization of the ventral semantic stream in humans: lessons from stimulation mapping in awake patients. *Front Syst Neurosci*. 2013;7:44. doi:10.3389/fnsys.2013.00044.

22. Khan OH, Herbet G, Moritz-Gasser S, Duffau H. The Role of Left Inferior Fronto-Occipital Fascicle in Verbal Perseveration: A Brain Electrostimulation Mapping Study. *Brain Topogr*. December 2013. doi:10.1007/s10548-013-0343-5.

23. Martino J, da Silva-Freitas R, Caballero H, Marco de Lucas E, García-Porrero JA, Vázquez-Barquero A. Fiber dissection and diffusion tensor imaging tractography study of the temporoparietal fiber intersection area. *Neurosurgery*. 2013;72(1 Suppl Operative):87-97; discussion 97-98. doi:10.1227/NEU.0b013e318274294b.

24. De Benedictis A, Duffau H, Paradiso B, et al. Anatomo-functional study of the temporo-

parieto-occipital region: dissection, tractographic and brain mapping evidence from a neurosurgical perspective. *J Anat*. 2014;225(2):132-151. doi:10.1111/joa.12204.

25. Duffau H. Is there a place for endoscopy in glioma surgery? *World Neurosurg*. 2014;82(6):1020-1022. doi:10.1016/j.wneu.2014.08.037.

Legends

Video1a. 00:00 Experimental setup. Magnetic landmarks were tacked up in a Klinger prepared right brain hemisphere. The tracker was inserted between the superior cerebellar surface and the tentorium, to which it was fixed with stiches. An elastic maintains the tracker in a rigid position. 00:13 The Axiem probe of the navigation system allows to trace the insular profile (corresponding to the anterior, superior and inferior insular sulcus) on the cortical surface. 00:23 1) Sylvian fissure (horizontal red line); 2) Superior temporal sulcus (horizontal blue line) 3) Pre-central sulcus (anterior vertical blue line); 4) Central sulcus (middle vertical blue line) and 5) Post-central sulcus (posterior vertical blue line). 00:35 Frontal view. 00:45 Identification of the precentral sulcus, confirmed by the neuronavigation system. 00:54. Ascending ramus of the sylvian fissure. 00:56 Horizontal ramus of the sylvian fissure. 01:00. Inferior frontal sulcus. 01:06 Incision and subpial dissection of pars triangularis. 01:15 White matter under the cortical surface of pars triangularis (U-fibers and IFOF terminations). 01:21 Identification of the point of intersection between the anterior and superior insular sulcus. 00:32 Temporal view. 01:35 Subpial dissection of the superior temporal gyrus. 01:47 Identification of the inferior insular sulcus. 02:00 A surgical corridor passing underneath the pial surface of the insula allows the communication between the frontal and the temporal operculum. 02:06 After removal of pars orbitalis and dissection of cortical insular surface, removal of insulo-opercular fibers. 02:12 Identification of a white matter bundle, corresponding to the inferior fronto-occipital fasciculus (IFOF) and the uncinate fasciculus (UF). 02:15 The neuronavigation system shows the topographic anatomy of this white matter's bundle, located in the anterior part of external/extreme capsule. 02:20 Further posterior dissection of the fiber bundle. 02:25. (Infero-)lateral view. Coronal cut within middle temporal gyrus. 02:33 Identification of the tip of the temporal horn. 02:38 Changing angle of view (looking from the front). C-shaped course of the UF towards the temporal pole. 02:48 Introduction of the neuronavigation probe from the frontal operculum up to the superior portion of the temporal stem. IFOF stem course in the superficial layer of the temporal stem. 02:53 The UF has been partly removed. 02:56 Dissection of the IFOF stem along the temporal stem. 03:03: Frontal view. Posterior course of the temporal stem constituting the roof of the temporal horn. Lateral displacement of this fiber bundle allows access to the temporal horn. 03:09 The navigation probe positioned on the putamen, located under the insular cortex, the extreme and the external capsule, posteriorly to the IFOF stem.

Video1b. Same as video1b, after image rotation, mimicking the surgical angle of view in the lateral positioning.

Video 2a. 00:00. Visualization of opercular region in the right hemisphere. 00:03 Incision of pars triangularis. 00:19 Initial subpial dissection of pars triangularis. 00:21 Termination of IFOF at the level of cortical surface of pars triangularis. 00:24 Additional removal of pars orbitalis, in order to achieve a wider surgical corridor. 00:28 Visualization of anterior insular sulcus. 00:31 Subpial dissection of the insula. 00:38 Frontal portion of IFOF underlying insular lobe. 00:46 Temporal pole resection. 00:58 Course of the IFOF, underneath the insular pial surface, from anteriorly (external capsule) to posteriorly (temporal stem in the roof of the temporal ventricle). 01:09 Lateral view of the temporal lobe: course of the sylvian fissure 01:13 Course of IFOF inside the temporal stem. 01:18 Surface of amygdala in front of the temporal horn. 01:21 Stretching the perforating arteries. 01:25 Anterior perforating substance, lying in the sphenoidal portion of the sylvian fissure 01:28 Anterior view of both frontal and temporal region 01:30 IFOF course. 01:32. Frontal pial membrane. 01:37 Choroid plexus. 01:40: Lateral surface of the temporal stem. 01:43 The frontal pial membrane is reversed towards the temporal side, showing the frontal course of the IFOF, which is overlying the putamen.

Video 2b. Same as video 2b, after image rotation, mimicking the surgical angle of view in the lateral positioning. Between 0:31 and 0:45, we kept the canonical angle of view, which is in fact close to the surgical view (the surgeon is looking from anterior to posterior, with an extreme oblique light angle).

Highlights :

- It is difficult to get familiar with the transopercular approaches of insula
- A laboratory model is propose to train subpial transopercular approaches
- Special emphasis is put on identification of surrounding fiber tracts

Abbreviation list : UF = uncinate fasciculus ; IFOF = inferior fronto-occipital fasciculus ; APS = anterior perforate substance ; MRI = magnetic resonance imaging ; SLF = superior longitudinal fasciculus ; LSA = lenticulo-striate artery ; MCA = middle cerebral artery ; DTI = diffusion tensor imaging